In the United States Court of Federal Claims

No. 12-477V

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K.T., a minor, by her mother and natural guardian, ALISHA DUDENHOEFFER, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	)	Vaccine Injury; Motion for Review; Causation-in-Fact; Measles-Mumps-Rubella ("MMR") Vaccine; Myclonic-Astatic Epilepsy ("MAE"); Epileptic Encephalopathy ("EE"); Molecular Mimicry

Clifford John Shoemaker, Shoemaker and Associates, Vienna, VA, for Petitioner.

Darryl R. Wishard, United States Department of Justice, Washington, DC, for Respondent.

OPINION AND ORDER

CAMPBELL-SMITH, Judge

Petitioner, Alisha Dudenhoeffer, seeks review of a decision in which the special master denied compensation for the claim she brought on behalf of her daughter, K.T. Petitioner alleges that K.T. developed the epileptic condition known as Myoclonic-

[1] Pursuant to Vaccine Rule 18(b) of the Rules of the United States Court of Federal Claims, this Opinion initially issued under seal to provide the parties the opportunity to object to the public disclosure of information contained within it. Neither party requested any redactions. The Opinion is thus reissued for publication in its entirety.

Astatic Epilepsy (MAE)[2] as a result of a measles, mumps, and rubella (MMR) vaccination K.T. received a few days after she turned one year old. K.T. is now eight years old.

On petitioner's motion, the court considers whether the special master's decision that petitioner was not entitled to compensation merits review. For the reasons set forth below, the court **DENIES** petitioner's motion for review and **SUSTAINS** the decision of the special master.

I. Background

A. Procedural History

In July 2012, petitioner filed a petition under the National Childhood Vaccine Injury Act of 1986 (Vaccine Act), codified as amended at 42 U.S.C. § 300aa-1 to -34 (2012), in which she alleged that the MMR vaccine K.T. received on August 6, 2009 caused her to suffer from a form of epilepsy. Pet. 2, ECF No. 1.

In September 2013, the Secretary of Health and Human Services, as respondent, filed a report recommending against compensation. Resp't's Report, ECF No. 32. Respondent asserted that petitioner had not proven by a preponderance of the evidence that the MMR vaccine caused K.T.'s condition. Id. at 11-17. Respondent added that petitioner had yet to present a medical theory linking the MMR vaccine to K.T.'s development of MAE. Id. at 13-16.

Between July 2012 and January 2013, petitioner filed a number of exhibits, including medical records (Exs. 1-15-2[3]), an expert report from Dr. Yuval Shafrir and his curriculum vitae (Exs. 16-17), as well as medical literature (Exs. 18-36, (references 1-19). Petitioner later filed additional medical records (Exs. 37, 58-62), two witness affidavits (Exs. 56-57), and a supplemental expert report from Dr. Shafrir (Ex. 38) with more medical literature (Exs. 39-55).

In April 2014, respondent filed exhibits A-K, including an expert report from Dr. Gregory Holmes and his curriculum vitae (Exs. A-B), as well as medical literature (Exs.

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[2] Myoclonic-Astatic Epilepsy is also known as "Doose Syndrome." Sarah A. Kelley & Eric H. Kossoff, Doose syndrome (myoclonic–astatic epilepsy): 40 years of progress, 52 Developmental Medicine & Child Neurology 988–993 (2010), Pet'r's Ex. 39 at 3; Hr'g Tr. (Tr.) 105, ECF No. 71.

[3] Exhibit 14 is a witness statement.

C-K). Respondent later filed a supplemental expert report from Dr. Holmes (Ex. L), and more medical literature (Exs. M-EE).

The special master held an entitlement hearing in December 2014. Dec. 2014 Hr'g Tr. (Tr.), ECF No. 71. Both parties' expert witnesses testified, Tr. 3, and the parties each filed post-hearing briefs setting forth their respective positions on entitlement. Pet'r's Br., ECF No. 77; Resp't's Br., ECF No. 74; Pet'r's Reply, ECF No. 77.

In September 2016, the special master issued a sealed decision denying compensation. ECF No. 84. Neither party proposed redactions and the special master publicly reissued her decision in October 2016.[4] ECF No. 87.

The special master determined that petitioner failed to prove that the MMR vaccine caused K.T.'s injury. Dec. 18, ECF No. 87. She further determined that the petitioner failed to establish a logical sequence of cause and effect between K.T.'s injury and her MMR vaccination. Id. at 21-22.

Petitioner moved for review of the special master's decision in October 2016. Pet'r's Mot., ECF No. 85. Petitioner claims that the special master denied compensation because she required a higher burden of proof than is required by Althen. Pet'r's Mot. 2; see also Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

Respondent filed a response in November 2016. Resp't's Resp., ECF No. 88. Respondent contends that the special master applied the correct burden of proof when she found petitioner's evidence to be unreliable and implausible. See Resp't's Resp. 12-19.

The court determined that oral argument on petitioner's motion was not necessary in light of the well-documented record. Order, ECF No. 89. The matter is ripe for ruling.

B. Evidence Before the Special Master

The special master's decision sets out – in significant detail – K.T.'s medical history, the qualifications of both parties' experts, and their respective opinions. See Dec. 2-8, 11-18. The court repeats here the factual and medical information pertinent to its review.

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[4] The special master's decision is available through commercial electronic databases. Dudenhoeffer v. Sec'y of Health & Human Servs., No. 12-477V, 2016 WL 5929954 (Fed. Cl. Spec. Mstr. Sept. 8, 2016).

1. Medical History[5]

For the first seven months following her birth on August 1, 2008, K.T. developed normally. Pet'r's Exs. 7 at 7; 15, at 111-23. She received 3 doses of the Haemophilus influenzae type b, Pediarix, Prevnar, and Rotateq vaccines, and one dose of Hepatitis B vaccine – without any apparent adverse reactions. Dec. 2.

K.T. experienced her first seizure and was taken to the hospital in April 2009. Dec. 2; Pet'r's Ex. 3 at 6. She was found to have suffered a febrile seizure. Dec. 2; Pet'r's Ex. 7 at 109-110. Later that same month, she had a well child check-up with her pediatrician, Dr. Voss. Pet'r's Ex. 9 at 123. No additional seizures were noted. Id.

Four months later, on August 6, 2009, K.T. had another pediatric office visit. Dec. 2; Pet'r's Ex. 15 at 100. At that one, she received Hepatitis A, Prevnar, and MMR vaccinations. Pet'r's Ex. 15 at 94-95.

Five days later, K.T. was seen at a medical clinic for thrush, and symptoms of the flu that included a loss of appetite, a sore throat, fevers, coughing, sneezing, and diarrhea. Dec. 2-3; Pet'r's Ex. 6 at 16. The nurse made note of a febrile seizure secondary to K.T.'s immunizations. Pet'r's Ex. 6 at 16.

K.T.'s mother took her to the hospital on August 18, 2009. Dec. 3; Pet'r's Ex. 7 at 183, 191-92, 196-200. Petitioner reported that K.T. had episodes of rolling her eyes upwards, dropping her arms, and becoming motionless and non-responsive. Pet'r's Ex. 7 at 196. She described K.T.'s seizures as occurring more frequently and lasting longer, over a period of 24 hours. Id.

K.T. was transferred to another hospital. Dec. 3; Pet'r's Ex. 11 at 3. There, her mother reported that she had "episodes of 'going blank' with her arms going limp to her sides for 5-15 seconds" at least once or twice per day from August 15 until August 17, 2009. Pet'r's Ex. 11 at 3. K.T.'s mother related that she had suffered 10 episodes within 20 minutes on August 18, 2009. Id. at 3, 13. K.T.'s mother added that K.T. had been "active and healthy other than a fever for about a week after [her] immunizations." Id. at 3.

The treating physician noted that K.T. had met all of her developmental milestones, and that she was "a very verbal child with good motor skills, per mom." Dec. 3; Pet'r's Ex. 11 at 13. The treating physician ordered an EEG to investigate whether

[5] The recited medical history is derived from the special master's decision, the parties' briefs, and the medical records filed by petitioner. See Dec. 2-8; Pet'r's Mot. 2-6, Resp't's Resp. 2-7; Pet'r's Exs. 1 to 15-2, 37, 58-62.

K.T.'s episodes were indicative of the onset of a seizure disorder. Dec. 3; Pet'r's Ex. 11 at 6, 16-18.

The EEG results showed an abnormal spike and a generalized wave pattern. Ex. 11 at 16. An MRI scan following sedation, however, did not reveal any structural abnormalities. Id. K.T. was referred to a neurologist and discharged with a prescription for Keppra. Id.; Dec. 4.

According to her mother, K.T. continued to experience episodes of unresponsiveness several times a day while taking Keppra – to include 15 occurrences in a single day. Dec. 4; Pet'r's Ex. 9 at 110-11. K.T. saw Dr. Facchini, a pediatric neurologist, who noted as part of the patient history that K.T. had experienced "a single generalized tonic-clonic seizure with fever" and "episodes of being unresponsive for a few seconds." Pet'r's Ex. 9 at 111.

When K.T. visited the Linn Clinic in November 2009, her mother reported that her episodes were occurring more frequently (20-40 times per day) and lasting longer (between 5-30 seconds each). Dec. 4; Pet'r's Ex. 6 at 15. During these episodes, K.T.'s eyes rolled backwards and her arms flopped at her sides. Pet'r's Ex. 6 at 15.

An EEG taken later in November 2009 revealed various abnormalities, including sharp waves in the right posterior temporal region and in the right and left central regions – as well as an axial tonic seizure in the right posterior temporal region. Dec. 4; Pet'r's Ex. 9 at 44. Dr. Facchini noted that K.T. appeared to be experiencing myoclonic-astatic seizures. Dec. 4-5; Pet'r's Ex. 9 at 47. Her nodding was consistent with such seizures. Pet'r's Ex. 9 at 47. Based on K.T.'s development and her MRI results, Dr. Facchini identified – on review of the telemetry – Benign Infantile Myoclonic Epilepsy and MAE as possible diagnoses. Pet'r's Ex. 9 at 47. But, he did not rule out the possibility of Dravet syndrome. Id.

Because K.T. was experiencing limited results with Keppra, she was prescribed Zonisamide. Dec. 5; Pet'r's Ex. 9 at 48. Her dosage was increased in February 2010, and she was placed on a ketogenic diet[6] after her mother reported that she was seizing for 5 to 10 seconds every 15 minutes. Dec. 5; Pet'r's Ex. 9 at 141.

Dr. Facchini diagnosed K.T. with likely MAE. Pet'r's Ex. 9 at 141. He noted that K.T.'s condition first presented as "a generalized tonic-clonic seizure during a febrile illness. Id.

K.T.'s mother sought additional medical opinions. In the Fall of 2010, she took K.T. to visit two more pediatric neurologists, namely Drs. Walsh and Gibbons. Dec. 5;

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[6] This is a special diet used primarily to treat epilepsy in children.

Pet'r's Ex. 10 at 8. Dr. Walsh noted that K.T. suffered from seizures and a "significant speech delay." Dec. 6; Pet'r's Ex. 10 at 11. K.T.'s EEG was found to be suggestive of epilepsy. Dec. 6; Pet'r's Ex. 10 at 10. K.T. was diagnosed with atonic seizures, prescribed Depakote, weaned off Zonisamide, and referred for a hearing exam and speech therapy. Dec. 6; Pet'r's Ex. 10 at 12.

Upon K.T.'s return visit to Dr. Walsh in July 2011, her mother reported that her seizures had ceased, but she was showing some language delay. Dec. 6; Pet'r's Ex. 10 at 18. During a subsequent visit to Dr. Walsh in January 2012, K.T.'s mother reported some speech improvement and no additional seizures. Dec. 6; Pet'r's Ex. 10 at 36.

During K.T.'s neurology visit six months later in June 2012, Dr. Gibbons noted that K.T. was still struggling with indistinct speech. Pet'r's Ex. 10 at 19-20. He opined that K.T. may have speech apraxia as well as symptomatic epilepsy. Id. But, he did not alter her treatment plan because K.T. was generally stable. Dec. 6-7; Pet'r's Ex. 10 at 20.

In a letter dated September 26, 2012, Dr. Voss wrote that K.T. "had a febrile seizure after she received the MMR vaccine as a one year old," and that – as her pediatrician – she recommended that "she not receive [any] further vaccines" until cleared by her neurologist to do so. Dec. 7; Pet'r's Ex. 12 at 1.

On examination of K.T. in February 2013, Dr. Gibbons – who was still treating her for neurologic issues – wrote that K.T.'s mother reported "[a] tremendous improvement in [K.T.'s] speech, and [that] she [was] much more understandable." Dec. 7; Pet'r's Ex. 37 at 6. Dr. Gibbons observed that K.T.'s mother was "convinced that [K.T.'s] seizures were somehow the result of an immunization she received at her 1 year visit to the pediatrician." Pet'r's Ex. 37 at 6. Dr. Gibbons disagreed with that proposition, stating that "without first-hand data from the time period surrounding her first event, it is impossible for us to corroborate such [a] relationship" between the received vaccine and the onset of K.T.'s seizures. Id. As to future vaccinations, Dr. Gibbons stated that:

> Given the typical age of onset of seizures generally occurring around the same age as childhood immunizations, it is difficult to identify [K.T.]'s vaccine as the likely cause of her epilepsy. Since we have no records from her initial presentation of seizure and we do not know the associated events, it is impossible for this office to affirm a medical contraindication for future immunizations. A more appropriate authority would be the physicians in charge of her care at the time of her first seizure presentation.

Dec. 7-8; Pet'r's Ex. 37 at 7.

2. The Expert Witnesses

a. Petitioner's Testifying Expert, Dr. Yuval Shafrir

Dr. Shafrir received his medical degree from Tel Aviv University in 1982. Pet'r's Ex. 17 at 1-3, ECF No. 35-3. He later completed a pediatric neurology residency at Washington University in St. Louis, and a pediatric epilepsy and neurophysiology fellowship at Miami Children's Hospital. Id. He subsequently served as associate professor at Georgetown University and the University of Oklahoma. Id. Dr. Shafrir is board-certified in neurology and clinical neurophysiology, with a special qualification in child neurology. Pet'r's Ex. 17 at 2; Tr. 67-68. Formerly board-certified in pediatrics, he has not renewed that certification due to the cost and time to do so. Id. Dr. Shafrir is now practicing as a private pediatric neurologist in Baltimore, Maryland. Pet'r's Ex. 17 at 3; Tr. 67. The special master admitted Dr. Shafrir at the hearing as an expert in the field of pediatric neurology, epilepsy, and interpreting EEGs. Tr. 68-70.

In both his expert report and his testimony, Dr. Shafrir expressed the opinion that the MMR vaccine K.T. received caused her injury. Dr. Shafrir proposed a diagnosis of MAE as well as epileptic encephalopathy (EE) for K.T. Tr. 110. He argued that an EE diagnosis is appropriate when either a "regression or a plateau" in cognitive or behavioral development occurs. Pet'r's Post Hr'g Mem. 13-14. Dr. Shafrir testified that K.T.'s display of "obvious encephalopathic symptoms" was indicative of EE. Tr. 110. Dr. Shafrir added that although K.T. met all of her developmental milestones before her August 2009 vaccination, the subsequent "stagnation of her development," as marked by an IQ score of 77 and the low expressive language score reflected in her individualized education plan, together with her mother's reports of motor and coordination problems, were the key factors tilting in favor of an EE diagnosis. Tr. 84. Having identified K.T.'s injury to include both MAE and EE, Dr. Shafrir reasoned that the MMR vaccine is able to cause such injuries through an adverse immunological response.

Of the possible immunologic responses to the MMR vaccine, Dr. Shafrir focused primarily on the process of molecular mimicry. Because petitioner's expert gave, at best, cursory attention to the bystander activation and epitope spreading theories, the court turns its attention – as did Dr. Shafrir – to consideration of the molecular mimicry theory of causation he offered. See Dec. 15-16.

According to the molecular mimicry theory posited by Dr. Shafrir, K.T.'s immune system failed to distinguish the antigenic determinants of the virus present in the MMR vaccine from K.T.'s own cells. Tr. 94, 101; Pet'r's Ex. 38, at 3-6 (citing Pet'r's Ex. 46 at 3, ECF No. 54-9 (Moshe Tishler & Yehuda Shoenfeld, Vaccines & Autoimmunity, The Autoimmune Diseases 309 (Noel R. Rose & Ian R. Mackay eds., 2006)). As support for that theory, Dr. Shafrir pointed to the known immunologic pathways leading to the development of autoimmune conditions such as experimental allergic encephalomyelitis, myasthenia gravis, and Guillain-Barré Syndrome. Pet'r's Ex. 38 at 3. Dr. Shafrir

endeavored to "provide the court with [a] presumed mechanism . . . solidly based on contemporary medical literature." Id.

Dr. Shafrir also posited that, in response to the MMR vaccine, K.T. could have developed antibodies to contactin-associated protein-like 2, known as "Caspr2." Id. at 6 (citing Pet'r's Ex. 45 at 3-6, ECF No. 54-8 (Demian F. Obregon et al., Potential Autoepitope within the Extracellular Region of Contactin-Associated Protein-like 2 in Mice, 4 British J. Med. & Med. R. 416 (2014)) (hereinafter "Obregon" with pincites to petitioner's pagination)); Tr. 100 (stating that the "appearance of antibodies against Caspr2 could be the cause of the onset of [K.T.'s] [injury]"). But, Dr. Shafrir acknowledged that the Obregon study on which he relied involved the pertussis virus, rather than the components of the MMR vaccine. Tr. 137. Dr. Shafrir cited to other studies to establish a link between Caspr2 and "autoimmune epilepsy, autoimmune encephalitis, and epilepsy and developmental regression."[7] Pet'r's Ex. 38 at 6. Dr. Shafrir offered each of the additional studies to demonstrate "a well-founded mechanism by which the MMR vaccine [could have] caused [K.T.'s] symptoms by induction of [an] autoimmune response to one [or] more of the protein[s] of the measles, mumps, and rubella viruses through a mechanism of molecular mimicry." Pet'r's Ex. 38 at 6.

Dr. Shafrir pointed to more studies and reports to support the theory that the MMR vaccine could be linked to the development of EE. Pet'r's Ex. 16 at 16-19. Among these materials was a comprehensive study linking the onset of an acute neurological illness to the measles vaccine. Id. at 16-17.[8] Another of the materials was a case study involving a child who developed Lennox-Gastaut syndrome, a form of EE, two weeks after receiving

[7] Citing Pet'r's Ex. 53 at 3-4, ECF No. 55-7 (James B. Lilleker et al., VGKC complex antibodies in epilepsy: Diagnostic yield and therapeutic implications, 22 Seizure 776 (2013)); Pet'r's Ex. 54 at 1, ECF No. 55-8 (Christopher J. Klein et al., Insights From LGI1 and CASPR2 Potassium Channel Complex Autoantibody Subtyping, 70 JAMA Neurology 229 (Feb. 2013)); Pet'r's Ex. 55 at 1, ECF No. 55-9 (Kevin A. Strauss et al., Recessive Symptomatic Focal Epilepsy and Mutant Contactin-Associated Protein-like 2, 354 New England J. Med. 1374 (2006)).

[8] Quoting Pet'r's Ex. 18, ECF No. 36-2 & 36-3 (R. Alderslade et al., The National Childhood Encephalopathy Study: A Report on 1000 Cases of Serious Neurological Disorders in Infants and Young Children from the NCES Research Team, in Whooping Cough: Reports from the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunisation, at 149 (U.K. Dep't of Health & Social Security ed., 1981)) (emphasis omitted).

a measles vaccination.[9] Id. at 19. Also among the materials was a series of studies that recorded abnormal EEGs following either a measles infection or a measles immunization.[10] Id. at 17-19.

b. Respondent's Testifying Expert, Dr. Gregory Holmes

Dr. Holmes received his medical degree from the University of Virginia in 1974 and he completed residencies at Yale University in pediatrics and at the University of Virginia in pediatric neurology. Resp't's Ex. B at 1, ECF No. 42-2; Tr. 157. Dr. Holmes is board-certified in clinical neurophysiology, pediatrics, and neurology (with a special competence in pediatric neurology). Resp't's Ex. B at 1; Tr. 158. He currently serves as the Chair of the Department of Neurological Sciences at the University of Vermont, College of Medicine, where he teaches and sees patients. Resp't's Ex. B at 2; Tr. 158-59. Dr. Holmes treats patients with epilepsy, epileptic seizures, EE, and MAE. Tr. 158-59. His primary focus of research has been EE, a subject about which he has published articles and book chapters and for which he has received awards. Id. at 160. The special master admitted Dr. Holmes as an expert in the field of pediatric neurology during the hearing. Id. at 161.

Dr. Holmes testified that it was "highly unlikely" that K.T.'s August 2009 MMR vaccination bore "any relationship whatsoever" to her subsequent seizure episodes. Tr. 185. He further testified that there was no "credible evidence" to "suggest that the MMR vaccine caused an autoimmune disease in [K.T.]." Id. at 186. Moreover, Dr. Holmes knows of no "convincing evidence" that the MMR vaccine can cause epilepsy or MAE; nor is he aware of any pediatric neurologists discussing such a theory in general. Id. at 188.

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[9] Citing Pet'r's Ex. 24, ECF No. 36-9 (Tatsuya Ishikawa et al., Lennox-Gastaut syndrome after a further attenuated live measles vaccination, 21 Brain & Development 563 (1999)).

[10] Citing Pet'r's Ex. 20, ECF No. 36-5 (G. Pampiglione et al., Transient Cerebral Changes After Vaccination Against Measles, The Lancet 5 (July 3, 1971)); Pet'r's Ex. 21, ECF No. 36-6 (G. Pampiglione, Prodromal Phase of Measles: Some Neurophysiological Studies, 2 British Med. J. 1296 (1964)); Pet'r's Ex. 22, ECF No. 36-7 (Frederic A. Gibbs & Ira M. Rosenthal, Electroencephalography in Natural and Attenuated Measles, 103 Am. J. of Diseases of Children 395 (Mar. 1962)); Pet'r's Ex. 23, ECF No. 36-8 (Frederic A. Gibbs et al., Electroencephalographic Abnormality in 'Uncomplicated' Childhood Diseases, 171 J. Am. Med. Ass'n 1050 (Oct. 1959))).

Addressing Dr. Shafrir's theory of molecular mimicry, and in particular his reliance on the Obregon study, Dr. Holmes testified that the study's authors found an increase in autoantibodies in the subject mice after creating a contrived environment that is not found naturally by administering lipopolysaccharide ("LPS") as well as the immunizing protein. Tr. 187. This dual administration had a dramatic effect. As Dr. Holmes explained, the LPS, in particular, acted to "destroy[] the brain" and, in so doing, created "a very artificial situation that doesn't reflect what happened to [K.T.] one bit." Id. Dr. Holmes added that the study's focus on autism, rather than on MAE or EE, diminished its relevance to this case. Tr. 224-27. Dr. Holmes observed that "it's a huge jump to look at [the Obregon study] and say [MAE] is caused by autoantibodies." Tr. 227.

Addressing several other studies and reports cited by Dr. Shafrir, Dr. Holmes noted that they "deal[t] with very small populations" and lacked "sufficient [statistical] power to result in any type of meaningful conclusions." Resp't's Ex. A at 6; see Tr. 190-92. Among the various problems Dr. Holmes identified in the studies and articles put forward by Dr. Shafrir was the marked difference between K.T.'s condition and the conditions at issue in the cited materials. Resp't's Ex. A at 5-6.

3. K.T.'s Diagnosis

The parties' experts agreed that: (1) K.T. suffers from MAE; (2) that MAE is generally regarded as a form of EE; and (3) that not all who suffer from MAE also have EE. But, the parties disagreed as to whether K.T. suffers from both EE and MAE. Dec. 11-12 (citing Pet'r's Post Hr'g Mem. 13-15; Resp't's Post Hr'g Br. 2-3); see also Tr. 105, 107, 163, 165. The special master held that petitioner proved by preponderant evidence that K.T. suffers from both MAE and EE, Dec. 18-19, and thereafter referred to K.T.'s injury as MAE, even when citing to evidence that addressed EE. See Dec. 13 (referring to MAE while citing to Tr. 100 which discusses EE instead).

Because MAE can occur in epileptic patients with EE, it is not clear that the special master's diagnostic determination was necessary. See Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1345 (Fed. Cir. 2010) (finding that a special master should determine what injury is in question based on the record evidence only if "the injury itself is in dispute, [and] the proposed injuries differ significantly in their pathology."). But, even if it were not necessary for the special master to have done so, the court is satisfied that the posited diagnostic determination was harmless error because the experts agree that the two conditions can be present in a patient. Moreover, Dr. Shafrir, as petitioner's expert, indicated that the theory of vaccine causation here is not dependent on either an EE or MAE diagnosis. Tr. 80-82. Thus, the court does not distinguish between the diagnoses here and refers to both MAE and EE when discussing the various records concerning K.T.'s injury.

II. Jurisdiction and Standard of Review

A. Motion for Review

On a motion for review of the special master's decision, this court has jurisdiction "to undertake a review of the record of the proceedings," and may take one of three actions:

> (A) uphold the findings of fact and conclusions of law of the special master and sustain the special master's decision,
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> (B) set aside any findings of fact or conclusion of law of the special master found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law, or
>
> (C) remand the petition to the special master for further action in accordance with the court's direction.

42 U.S.C. § 300aa–12(e)(2); see also Vaccine Rule 27. The Federal Circuit has instructed that: "Fact findings are reviewed . . . under the arbitrary and capricious standard; legal questions under the 'not in accordance with law' standard; and discretionary rulings under the abuse of discretion standard. The latter will rarely come into play except where the special master excludes evidence." Munn v. Sec'y of Health & Human Servs., 970 F.2d 863, 870 n.10 (Fed. Cir. 1992).

When reviewing a special master's determination as to "whether the evidence submitted by the petitioner warranted a conclusion that the vaccine caused the injury," the court applies an "arbitrary and capricious" standard. Hines v. Sec'y of Health & Human Servs., 940 F.2d 1518, 1527 (Fed. Cir. 1991).

> The arbitrary and capricious standard of review is difficult for an appellant to satisfy with respect to any issue, but particularly with respect to an issue that turns on the weighing of evidence by the trier of fact. In general, reversible error is "extremely difficult to demonstrate" if the special master "has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision."

Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357, 1360 (Fed. Cir. 2000) (quoting Hines, 940 F.2d at 1528). When a party provides

> testimony [that] supports the special master's finding on [a] point, . . . although [the opposing party may] contend that the more compelling

> evidence is to the contrary, we do not sit to reweigh the evidence. [To the extent that] the special master's conclusion was based on evidence in the record that was not wholly implausible, [the reviewing court is] compelled to uphold that finding as not being arbitrary or capricious.

Id. at 1363. The reviewing court does not "examine the probative value of the evidence or the credibility of the witnesses. These are all matters within the purview of the fact finder." Munn, 970 F.2d at 871.

B. Proving Causation Under the Vaccine Act

Pursuant to 42 U.S.C. § 300aa-13(a)(1), the court must award compensation to a petitioner who proves all of the elements set forth in Section 300aa-11(c)(1), and who establishes that the claimed illness is not due to factors unrelated to the administration of the vaccine. A petitioner can recover either by proving an injury listed on the Vaccine Injury Table (Table) or by proving causation-in-fact. See 42 U.S.C. §§ 300aa-11(c)(1)(C), -13(a)(1).

Because K.T. did not suffer a Table Injury, her mother must prove causation in fact. See 42 U.S.C. § 300aa-11(c)(1)(C) (2012). To establish such a case, "petitioner [must] prove, by a preponderance of the evidence, that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352 (Fed. Cir. 1999). "[T]o show that the vaccine was a substantial factor in bringing about the injury, the petitioner must show 'a medical theory causally connecting the vaccination and the injury.'" Id. at 1352-53 (quoting Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992) (per curiam)). Stated another way, "[t]here must be a 'logical sequence of cause and effect showing that the vaccination was the reason for the injury,'" id. at 1353 (quoting Grant, 956 F.2d at 1148), and "[t]his logical sequence of cause and effect must be supported by a sound and reliable medical or scientific explanation." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548 (Fed. Cir. 1994) (internal quotation marks omitted); see also 42 U.S.C. § 300aa-13(a)(1) ("The special master or court may not make such a finding based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion."). Medical or scientific certainty, however, is not required. Knudsen, 35 F.3d at 548-49.

In Althen v. Sec'y of Health & Human Servs., the Federal Circuit distilled this precedent into a three-part test, holding that to prove causation-in-fact, a petitioner must provide: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278. These three prongs "must cumulatively show that the vaccination was a 'but-for' cause of the harm, rather than just an insubstantial contributor

in, or one among several possible causes of, the harm." Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006).

Once a petitioner has established a prima facie case, the burden shifts to the respondent to show, by a preponderance of the evidence, that the injury was caused by a factor unrelated to the vaccine. 42 U.S.C. § 300aa-13(a)(1)(B); Shalala v. Whitecotton, 514 U.S. 268, 270-71 (1995); de Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008). If the petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Human Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993). Whether or not the burden ever shifts to the respondent, the special master may consider the evidence presented by the respondent in determining whether the petitioner has established a prima facie case. See Stone v. Sec'y of Health & Human Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan, 539 F.3d at 1353 ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case-in-chief.").

III. Discussion

Petitioner claims that the special master acted arbitrarily and capriciously when she:

> impermissibly raised K.T.'s burden of proof by requiring confirmation or probability of the validity of the specific theory of causation in the medical literature and direct evidence of how the MMR vaccine caused epileptic encephalopathy, MAE, or Doose Syndrome rather than mere "reliability" or "plausibility" as required by prong 1 of Althen and required affirmative opinions of treating doctors rather than simply a logical sequence of cause and effect linking the vaccine to the injury as required by prong 2 of Althen.

Pet'r's Mot. 2 (discussing Althen, 418 F.3d at 1278).

The court considers petitioner's challenges to the special master's Althen analysis – particularly under prongs 1 and 2. Petitioner does not challenge the special master's Althen prong 3 analysis, but does contest the special master's findings under Althen prong 2 – based, in-part, to the special master's affirmative finding that a temporal association had been established under prong 3. For this reason, the court reviews the special master's findings as to prong 1 independently and as to prongs 2 and 3 jointly. As set forth below, the court finds that petitioner failed to meet her burden of proof under the Althen standard.

A. Althen prong 1

Under the first prong of Althen, a petitioner must show that it is more likely than not that the received vaccine can cause the alleged injury. See Pafford, 451 F.3d at 1355-56. The first prong of Althen "requires that petitioners . . . provide a 'reputable medical or scientific explanation" for their claim.'" Cozart v. Sec'y of Health and Human Servs., 126 Fed. Cl. 488, 498 (2016) (quoting Althen, 418 F.3d at 1278). Petitioner's theory must be "legally probable, [but] not medically or scientifically certain." Knudsen, 35 F.3d at 549. The special master may conclude that a medical opinion or theory is unreliable where "there is simply too great an analytical gap between the data and the opinion proffered." Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1339 (Fed. Cir. 2010) (quoting Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997)).

1. The Special Master Applied the Correct Legal Standard in Determining that Petitioner's Medical Theory Linking K.T.'s MMR Vaccination to Her Injury Was Not Persuasive

Petitioner argues that prong 1 of Althen requires "mere 'reliability' or 'plausibility,'" rather than the "more likely than not" standard applied by the special master. Pet'r's Mot. 16. Petitioner claims that, as applied, the legal standard was heightened to require either "confirmation [of] or [a] probability of . . . validity" of Dr. Shafrir's theory, as well as "direct evidence" as to how the MMR vaccine is able to cause the epileptic condition of either MAE or EE. Pet'r's Mot. 11, 16. Relying on Althen, petitioner asserts that this legal requirement is too much because, "the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body." Pet'r's Mot. 14 (citing Althen, 418 F.3d at 1280).

Respondent argues that petitioner effectively asks the court to find "the opinion offered by Dr. Shafrir [to be] per se reliable." Resp't's Resp. 14. But, respondent asserts, "the special master is not required to simply accept an expert's opinion ipse dixit." Id. Respondent contends that the special master here performed a careful and thorough evaluation of Dr. Shafrir's theory that the MMR vaccine could cause either MAE or EE through molecular mimicry. Id. (citing Dec. 12-16, 19-21).

The court agrees with defendant and finds petitioner's assertions to the contrary to be without merit. The special master heard the testimony of two well-qualified experts offering contradictory opinions as to vaccine causation. In evaluating the reliability of the experts' testimony, the special master properly considered the scientific literature upon which the experts relied. Dec. 16; see also Caves v. Sec'y of Health & Human Servs., 100 Fed. Cl. 119, 133-34 (2011) (finding that an expert may opine without the support of medical literature, but such opinion is rarely persuasive).

Petitioners argue that the special master failed to consider the medical literature "as a whole." Pet'r's Mot. 15-16. Yet, the special master found that the evidence petitioner put forward, "whether considered in isolation or in concert," did not provide either reliable or persuasive support for a causal link between Caspr2 and MAE which was a critical component of petitioner's expert's molecular mimicry theory. Dec. 21. The special master also found that respondent's expert persuasively called into question the limitations of the Obregon study, upon which petitioner's expert hung his theory of molecular mimicry. Dec. 20-21. She noted that "even the authors of the [Obregon study] [went] to great lengths to point out the limited inferences that one can draw from its findings . . ." and found the article "insufficient to serve as the only medical literature purporting to link the MMR vaccination and MAE." Id. at 21. Under the arbitrary and capricious standard of review, "the court may not reweigh the evidence if the special master has 'considered the relevant evidence of record, drawn plausible inferences, and articulated a rational basis for [her] decision.'" Dobrydnev v. Sec'y of Health & Human Servs., 566 F. App'x 976, 984 (Fed. Cir. 2014) (quoting Hazlehurst v. Sec'y of Health & Human Servs., 604 F.3d 1343, 1349 (Fed. Cir. 2010).

Contrary to petitioner's assertion, the special master did not apply a heightened legal standard. Pet'r's Mot. 11, 16. The special master considered the evidence before her and properly applied the preponderant evidence standard in evaluating whether petitioner showed that "more likely than not" the MMR vaccine can cause either MAE or EE. Dec. 10.

The court finds that the special master's decision under Althen prong 1 was supported by evidence in the record.

B. Althen prongs 2 and 3

The second prong of Althen requires that petitioner show by preponderant evidence a "logical sequence of cause and effect showing that the [administered] vaccination was the reason for [petitioner's] injury." Pafford, 451 F.3d at 1355-56 (citing Althen, 418 F.3d at 1278). Petitioner may satisfy this prong with medical opinion alone, id.; but the special master may require "some indicia of reliability to support the assertion of the expert witness." Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1324 (Fed. Cir. 2010) (citing Terran v. Sec'y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999)).

To satisfy the third prong of Althen, a petitioner must provide preponderant evidence of "a proximate temporal relationship between vaccination and injury." Pafford, 451 F.3d at 1355 (citing Althen, 418 F.3d at 1278). To accomplish this, petitioners must demonstrate "that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The medically

accepted timeframe proffered by petitioner must coincide with petitioner's medical theory of causation. Id.; Shapiro v. Sec'y of Health & Human Servs., 101 Fed. Cl. 532, 542 (2011). Although temporal proximity is a factor to be considered in the analysis of causation under Althen prong 3, "a proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury," as is required under Althen prong 2. Grant, 956 F.2d at 1148.

1. The Special Master Applied the Correct Legal Standard in Finding that Petitioner Failed to Establish a Logical Sequence of Cause and Effect Between K.T.'s Injury and Her MMR Vaccination

Petitioner contends that the special master erred by "requir[ing] affirmative opinions of [causation from] treating doctors rather than simply [accepting as] logical [the proposed] sequence of cause and effect linking the vaccine to the injury." Pet'r's Mot. 1-2. While petitioner asserts that the Federal Circuit does not "require the support of a treating doctor for a finding of causation," petitioner acknowledges that "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" Pet'r's Mot. 18-19 (quoting Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1326 (Fed. Cir. 2006)). Here, petitioner insists that "the medical records themselves demonstrate a clinical picture that fits the theory espoused by Dr. Shafrir as to the onset and development of the epileptic encephalopathy as well as the medically appropriate onset of symptoms as established in both the NCES and the vaccine injury table." Pet'r's Mot. 19.

Respondent argues that the special master properly found that petitioner failed to "provide reliable, persuasive evidence that the MMR vaccination actually caused KT's EE or MAE." Resp't's Resp. 19. Respondent noted that "Dr. Shafrir failed to provide any support for Althen prong two, beyond rehashing his opinions on the medical theory and [pointing to] the temporal proximity between the vaccine and KT's symptom onset." Id.

The special master afforded petitioner the opportunity to present circumstantial evidence and reliable medical opinions. But, contrary to petitioner's assertions, the special master did not require her to offer any particular type of evidence such as – "'epidemiologic studies, rechallenge, presence of pathological markers or genetic disposition, or general acceptance in the scientific and medical communities' to establish a logical sequence of cause and effect." Dec. 11 (quoting Capizzano, 440 F.3d at 1322).

Having heard from petitioner's expert witness, Dr. Shafrir, the special master found his testimony to be inadequate. The special master commented that he "hardly discussed Althen's second prong at the hearing." Dec. 22. She noted that to the extent he did, he "merely restated his theory of causation and inserted K.T.'s name." Id.

Although petitioner asserts otherwise, the special master did not require that she provide a causation opinion from one of K.T.'s treating physicians. Pet'r's Mot. 1-2. The special master did, however, consider the statements of K.T.'s treating physicians, noting that "none of K.T.'s [earliest] treating physicians linked her vaccination and injury." Dec. 22. Rather, in September 2012 – nearly three years after K.T. received the MMR vaccination at issue – her treating pediatrician, Dr. Voss, recommended that she "not receive [any] further vaccines" until a neurologist cleared her to do so. Dec. 7; Pet'r's Ex. 12 at 1. But, K.T.'s neurologist, Dr. Gibbons, clearly did not share Dr. Voss's expressed concerns. Compare Pet'r's Ex. 12 at 1, with Pet'r's Ex. 37 at 7. Instead, Dr. Gibbons remarked, it was petitioner herself who seemed "convinced that [K.T.'s] seizures were somehow the result of an immunization she received at her 1 year visit to the pediatrician." Pet'r's Ex. 37 at 6-7. Dr. Gibbons did not share petitioner's conviction, nor agree with her. Id.

Weighing the evidence before her, the special master found that "Dr. Voss's letter advising against future vaccines [was], at best, offset by Dr. Gibbons's statements opining against causation." Dec. 11; see Pet'r's Ex. 37 at 7 (Dr. Gibbons's statement that there was insufficient evidence to link the MMR vaccination with K.T.'s epilepsy condition); Tr. 47. As respondent correctly pointed out in its briefing, "[K.T.'s] primary care physician (Dr. Voss) deferred to [her neurology] specialist (Dr. Gibbons) on [the issue of] further vaccination . . . and the specialist saw no evidence to support vaccine causation and no good reason to further defer KT's childhood vaccinations." Resp't's Resp. 19 (citing Pet'r's Ex. 37 at 6-7). The court finds no error in the legal standard applied by the special master.

2. The Special Master Applied the Correct Legal Standard in Finding that A Temporal Association Alone is Not Enough to Establish Vaccine Injury Causation

The special master found that "K.T.'s MAE began nine days after the MMR vaccination." Dec. 22. Petitioner does not contest the special master's Althen's prong 3 findings. Rather, she points to these findings to support her claim that the special master erred in her Althen prong 2 analysis. Petitioner calls into question the special master's rejection of K.T.'s claim under Althen prong 2, because the special master found in her favor under Althen prong 3. Pet'r's Mot. 17.

Petitioner, however, incorrectly conflates prongs 2 and 3 of Althen. The special master applied the correct legal standard when considering the second and third prongs of Althen. The special master determined that "the temporal proximity between the vaccination and the claimed injury is a factor to be considered under Althen's second prong; however, temporal association alone [was] insufficient to satisfy that prong." Dec. 11 (internal citations omitted). Thus, the special master's finding under Althen

prong 3 – that petitioner proved a temporal association – did not preclude the finding that petitioner failed to meet her burden under Althen prong 2.

The record supports the special master's findings under Althen prong 2 and the inferences she drew from the evidence. And, because petitioner has failed to meet her burden of proof under Althen prong 1 and prong 2, the court need not review the special master's findings as to prong 3 of Althen any further. Moberly, 592 F.3d at 1323 ("a proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury").

On review, the court concludes that the special master's finding were supported by the record before her and thus, it declines to disturb the special master's decision.

IV. Conclusion

For the reasons set forth above, the court **DENIES** petitioner's motion for review and **SUSTAINS** the decision of the special master. The Clerk of the Court shall enter judgment accordingly.

IT IS SO ORDERED.

s/ Patricia Campbell-Smith
PATRICIA CAMPBELL-SMITH
Judge